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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,893	09/16/2005	Shigeo Yanai	68115(46590)	7166

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
11/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,893	YANAI ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 07/10/09 are acknowledged.

2. Claims 1-22, 24-26, and 28-35 were cancelled.

3. Claim 23 was amended.

4. Claims 23 and 27 are included in the prosecution.

Response to Arguments

Rejection of claims 23 and 27 under 35 USC § 103(a)

5. Applicant's arguments, see Page 3, filed 07/10/09, with respect to the rejection of claims 23 and 27 under 35 USC § 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Mazer et al. (US 5,160,742) have been fully considered and are persuasive in light of the amendment of claim 23. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection are made over Tasaka et al. (WO 02/40484) in view of Mazer et al. (US 5,160,742) and further in view of Samejima et al. (US 5,068,112).

NEW REJECTIONS:

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Mazer et al. (US 5,160,742) and further in view of Samejima et al. (US 5,068,112).

The claimed invention is a controlled release composition for oral administration, wherein

(A) a core containing

(1) (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide or a salt thereof, and

(2) a hydrophilic polymer selected from hydroxypropylcellulose and low-substituted hydroxypropylcellulose, wherein

an in inert carrier particle is coated with a coating layer comprising

(1) (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide or a salt thereof, and

(2) a hydrophilic polymer selected from hydroxypropylcellulose and low-substituted hydroxypropylcellulose, which is coated with

(B) a coating layer containing

(1) methacrylic acid copolymers as an enteric coating agent,

(2) talc as a lubricant, and

(3) a plasticizer selected from polyethylene glycol and triethyl citrate,

wherein the core is in a granule form having the average particle diameter of from about 50 to about 2000 μm.

Tasaka teaches a compound of the formula:

(I)

wherein n is an integer of 1 to 3; and Ar is an optionally substituted aromatic ring, or a salt thereof (Page 4, lines 1-8). The compound (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide is disclosed as one of the compounds (Page 6, lines 24-25). A pharmaceutical composition containing the compound, which is an antitumor agent, and which is an agent for the prophylaxis or treatment of breast cancer or prostate cancer is disclosed (Page 8, lines 6-14). Pharmaceutically acceptable carriers that are used in the composition, including an excipient, a lubricant, a binder, a disintegrating agent and a thickener are disclosed (Page 39, lines 29-33). "Preferable examples of the excipient include lactose, sucrose, D-mannitol, starch, ... Preferable examples of the lubricant include magnesium stearate, calcium stearate, talc, colloidal silica ... Preferable examples of the binder include ... hydroxypropylcellulose, hydroxypropylmethylcellulose ... Preferable examples of the disintegrating agent include starch, carboxymethyl cellulose, carboxymethyl cellulose calcium, crosscarmellose sodium, sodium carboxymethyl starch ... Preferable examples of the thickener include natural gums ... Preferable examples of the solvent include ... propylene glycol ... Preferable examples of the dispersing agent include polyethylene glycol ... Preferable examples of the solubilizer include polyethylene glycol, propylene glycol ... Preferable examples of the isotonicity agent include ... glycerine ..." (Page 40, lines 4-33). The reference also discloses that a

tablet, powder, granule or capsule can be prepared by adding "an excipient, a disintegrating agent, a binder, a lubricant and the like to the compound of the present invention, and subjecting the mixture to compression molding, and where necessary, coating for masking of taste, enteric coating or coating for sustention" (Page 41, lines 12-18). The pharmaceutical preparation can be administered orally (Page 42, lines 26-28) and a sustained release preparation can also be administered (Page 43, lines 8-9). Example 5 discloses the production of 6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide (Page 58, line 12 to Page 59, line 8).

Tasaka does not teach methacrylic acid copolymers as enteric coating agents and the granules having an average particle diameter of from about 50 to about 2000 μm. Tasaka does not expressly teach an inert carrier particle that is coated with a coating layer comprising a drug and a hydrophilic polymer.

Mazer teaches a system for delivering an active substance with sustained release of the active substance in the intestinal tract (Abstract). The active compound and one or more excipients are formed into a core and coated (Col. 5, lines 42-49). Enteric coating materials of the core particles include methacrylic acid copolymers (Col. 8, lines 15-25). A plasticizer component for the enteric coat component includes triethyl citrate (Col. 8, lines 43-51). An anti-tackiness agent for the enteric coat component comprises talc (Col. 8, lines 52-53). The enteric coating (along with the plasticizer and the anti-tackiness agent) is applied to the core (Col. 10, lines 9-23). The active ingredient granular cores have a particle size range of about 177-420 microns (Col. 10, lines 57-59).

Samejima teaches that a core can be prepared "according to the rotating granulation method, the pan coating method, the fluidized bed coating method, etc. in which a pharmaceutical compound or a mixture of the compound with an excipient or excipients is added little by little to inert carrier particles while spraying a solution of a binder dissolved in a suitable solvent ... on the surface of inert carrier particles. In this case, as the inert carrier particles, for example, those prepared from sucrose, lactose, starch, crystalline cellulose, etc. may be suitably employed. Such carrier particles should preferably have an average particle size of about 300 μm to about 1500 μm" (Col. 5, lines 26-52).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and an enteric coating, as suggested by Tasaka, combine it with the enteric coating (comprising methacrylic acid copolymers, plasticizer, and anti-tackiness agent) of core particles in the particle size of about 177-420 microns, as taught by Mazer, further use the preparation of a core particle by coating inert carrier particles with a solution containing a pharmaceutical compound and excipients, as taught by Samejima, and produce the instant invention.

One of ordinary skill in the art would do this because methacrylic acid copolymers are known components of enteric coatings, as evidenced by the enteric coating taught by Tasaka (Page 41, lines 12-18) and by the enteric coating of core granules as taught by Mazer (Col. 8, lines 15-25). One of ordinary skill in the art would use the active compound and hydroxypropylcellulose granule of Tasaka and coat these

granules with the enteric coating taught by Mazer, with a reasonable expectation of success in producing a controlled release composition with granules of compound of formula (1)-A. Simple substitution of one known element for another to obtain predictable results. See MPEP 2141.

Furthermore, one of ordinary skill in the art would use the preparation of core particles by coating inert particles with a solution containing a pharmaceutical compound and excipients because Samejima discloses such a technique as one that is conventional in the art (Col. 5, lines 26-52). MPEP 2141 states that use of a known technique to improve similar devices (methods or products) in the same way is obvious. All references teach controlled release compositions and the inclusion of the pharmaceutical compound in the core particle. It would be obvious to one of ordinary skill in the art to combine the teachings of Tasaka, Mazer and Samejima and obtain predictable results, i.e., producing a functional controlled release product.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 23, the controlled release composition is taught by the composition comprising the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The core containing (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide would have been obvious over

the compound (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide disclosed by Tasaka (Page 6, lines 24-25). The limitation of an inert carrier particle coated with a coating layer comprising (+)-6-(7-hydroxy- 6, 7-dihydro-5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide would have been obvious over the teaching of the compound (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide disclosed by Tasaka (Page 6, lines 24-25) in view of the preparation of a core particle by coating inert carrier particles with a solution containing a pharmaceutical compound and excipients, as taught by Samejima (Col. 5, lines 26-52). The hydrophilic polymer would have been obvious over the hydroxypropylcellulose taught by Tasaka (Page 40, lines 8-10). The enteric coating would have been obvious over the enteric coating taught by Tasaka (Page 41, lines 12-18) and by the enteric coating taught by Mazer (Col. 8, lines 15-25). The methacrylic acid copolymers for enteric coating would have been obvious over the enteric coating materials including methacrylic acid copolymers, as taught by Mazer (Col. 8, lines 15-25). The limitation of talc as a lubricant, and triethyl citrate as the plasticizer would have been obvious over the triethyl citrate plasticizer (Col. 8, lines 43-51), and talc as the anti-tackiness agent (Col. 8, lines 52-53) in the enteric coating, as taught by Mazer. The limitation of the particle diameter of the core granules of from about 50 to about 2000 μm would have been obvious over the granular cores having a particle size range of about 177-420 microns, as taught by Mazer (Col. 10, lines 57-59).

Regarding instant claim 27, the use of the controlled release composition for treating prostate cancer or breast cancer would have been obvious over the

pharmaceutical composition used for the treatment of breast cancer or prostate cancer as taught by Tasaka (Page 8, lines 6-14). Moreover, the use of the controlled release composition for "prevention" of prostate cancer or breast cancer is an intended use and has no significance in composition claims.

Conclusion

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615